Advanced: Tumors and Their Interactions with the Microenvironment

Overview

Students learn about a real research project that examined tumor growth in relation to a low-oxygen microenvironment. The virtual lab —"Can tumors be starved to death?"—allows students to go step-by-step through the experiments and draw conclusions based on simulated results. Very advanced students may attempt to read the published article, which expands on the methods used and describes additional findings. This lesson addresses the Next Generation Science Standards (NGSS) Performance Expectation HS-LS1-4. View the standards that apply to this unit.

Important Terminology

Teratoma: a type of tumor created from the injection of embryonic stem cells into a rodent. This tumor contains cell types from all three germ layers of the embryo because the original cells were pluripotent. Cells of unknown potency can be injected into a rodent, and if a teratoma forms, the researcher now knows the cells are pluripotent.

Transcription factor: in response to an environmental signal such as stress, proteins called transcription factors bind to the promoter/enhancer regions of many genes to change (increase, decrease) mRNA production. This usually leads to a concomitant increase or decrease in protein production and a change in cell behavior. Stem cell phenotype is often maintained by transcription factors known as "stemness" genes.

For more information, see Teacher Background Information 3 from CIRM model stem cell curriculum Unit 3.

Outline of Lesson

Discussion of homework
Students can show each other their breast cancer development drawings in groups.

1. Group representative explains the group's chosen drawing to the class.

Introduction to Virtual lab activity

1. This lab is based on actual research from the University of California, San Diego.
2. The ultimate goal of this type of research is to find a way to stop nutrients and oxygen from being delivered to solid tumors, like those that form in breast cancer.
3. When a tumor grows, cells in the middle become starved of oxygen (hypoxic) because there are not enough capillaries to feed the tumor. The cells begin the process of gene expression, eventually leading to an increase in capillaries that support the growing tumor.
4. This project specifically pinpointed two proteins involved in capillary growth.

    a. One protein acts inside the cell; Hypoxia-inducible transcription factor (HIF-1) is expressed when the cell senses a decrease in microenvironmental oxygen levels. Transcription factors control the expression of many genes that help cells respond to low oxygen.
    b. One protein acts outside of the cell; Vascular endothelial growth factor (VEGF) causes capillaries to grow and support the tumor.

5. The researchers used mutated Embryonic Stem Cells—that form tumors when injected into mice without immune systems—deficient in HIF-1 and examined the size of the tumors over time.
6. Explore the virtual lab to see what happened.
7. While you do the activity, write down the different interactions between the cells and their microenvironment. *Teacher example: Oxygen-starved tumor cells produce VEGF, which causes capillary cells to proliferate. This demonstrates cell-cell interaction through a soluble factor.*

Virtual lab activity: Can tumors be starved to death?

Homework assignment—teacher can choose appropriate readings from the following list, organized by type of microenvironmental influence and difficulty. Students can summarize the articles in a way that integrates the components of the microenvironment: signaling factors, extracellular matrix proteins, forces, and cell-cell interactions. Cite the articles in the text as well as in a references section.

Signaling factors

1. EASY Science Daily: Key Mechanism That Regulates Development Of Stem Cells Into Neurons Identified
2. EASY Science Daily: Finnish Scientists Discover Nerve Growth Factor With Therapeutic Potential In Parkinson's Disease
3. MID Science Daily: Why Neural Stem Cells Divide and Differentiate
4. HARD Science Daily: How Stem Cells Make Skin

Extracellular Matrix Proteins

1. EASY Science Daily: Potential Therapy For Congenital Muscular Dystrophy
2. MID Science Daily: Molecule that Coordinates the Movement of Cells Identified
3. MID Description of research, Engler Lab, UC San Diego
4. MID Sigma-Aldrich: Why Optimize ECM?
5. HARD Role of Extracellular Matrix Factors in Stem Cell Differentiation Supported by Reports in Stem Cells and Development

Forces

1. EASY University of California: UC Berkeley bioengineer to receive NIH New Innovator Award
2. MID Phys.org: Small mechanical forces have big impact on embryonic stem cells
3. MID Science Daily; Modeling Cell Division: How A Cell Interacts With Its Microenvironment

Cell-cell interactions

1. MID Science Daily: Receptor Also Active Inside the Cell
2. HARD Science Daily: Functional Differences Discovered Between Two Integrins In Adhesion Of The Cell To Its Environment
3. HARD Molecular and Systems Biology research article: Cell-cell Interaction Works to Regulate Blood Stem and Progenitor Cell Fate

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